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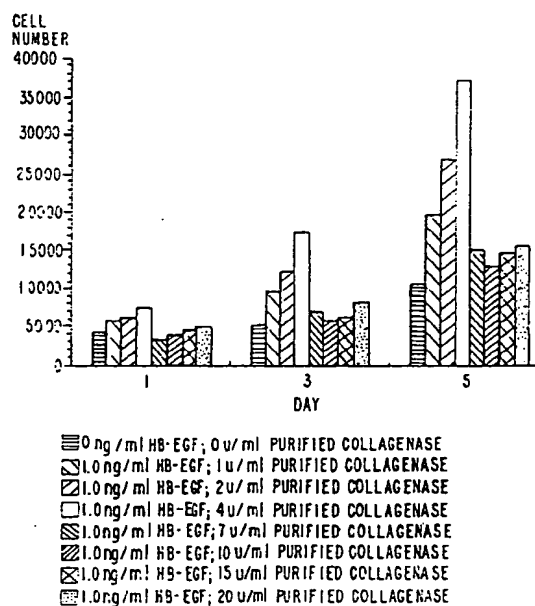
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(54) Enhancing keratinocyte migration and proliferation

(57) A method of enhancing the migration and proliferation of keratinocytes in wound healing or in the growth of artificial skin grown in vitro. The wound is contacted with (a) an effective amount of purified Clostridiopeptidase A collagenase that is substantially free from other proteinases and (b) an amount of a growth factor that increases the effects of said collagenase. The artificial skin is grown upon biomatrices previously synthesized by living cells and digested with Clostridiopeptidase A collagenase while in the presence of (a) an effective concentration of purified Clostridiopeptidase A collagenase substantially free from other proteinases and (b) a growth factor in a concentration effective to increase the effectiveness of said collagenase.

FIG. 8



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# EUROPEAN SEARCH REPORT

Application Number  
EP 97 31 0407

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
X	EP 0 637 450 A (COLLAGEN CORPORATION) 8 February 1995 * column 6, lines 7-24 *	1-5,7-15	A61K38/48 C12N5/08 //(A61K38/48, 38:18)
X	WO 93 06802 A (ROLF, D. ) 15 April 1993 * claim 27; p. 26-27, items 54 and 60-63 *	1-5,7-18	
Y,D	HERMAN, I.: "Stimulation of human keratinocyte migration and proliferation in vitro: ..." WOUNDS, vol. 8, no. 2, March 1996, pages 33-41, XP002097766 * whole disclosure *	1-18	
Y	MATSUMOTO, K. ET AL.: "Marked stimulation of growth and motility of human keratinocytes by hepatic growth factor" EXP. CELL RES., vol. 196, 1991, pages 114-120, XP002097767 * abstract *	1-18	
A	WO 96 28543 A (KNOLL AG) 19 September 1996 * claims 6 and 7 *	1-18	<div>TECHNICAL FIELDS SEARCHED (Int.Cl.6)</div> <div>C12N A61K</div>
The present search report has been drawn up for all claims			
Place of search MUNICH		Date of completion of the search 24 March 1999	Examiner Hermann, R
<div>CATEGORY OF CITED DOCUMENTS</div> <div> X : particularly relevant if taken alone  Y : particularly relevant if combined with another document of the same category  A : technological background  O : non-written disclosure  P : intermediate document  T : theory or principle underlying the invention  E : earlier patent document, but published on, or after the filing date  D : document cited in the application  L : document cited for other reasons  &amp; : member of the same patent family, corresponding document </div>			

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ON EUROPEAN PATENT APPLICATION NO.**

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The members are as contained in the European Patent Office EDP file on  
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24-03-1999

Patent document cited in search report		Publication date		Patent family member(s)		Publication date
EP 637450	A	08-02-1995	CA	2103938 A		05-02-1995
			JP	7089867 A		04-04-1995
-----						
WO 9306802	A	15-04-1993	US	5804213 A		08-09-1998
			AU	663737 B		19-10-1995
			AU	2785792 A		03-05-1993
			CA	2120936 A		15-04-1993
			EP	0625894 A		30-11-1994
			FI	941627 A		08-06-1994
			JP	7500035 T		05-01-1995
			MX	9205848 A		01-05-1993
			NO	941284 A		08-06-1998
			ZA	9207749 A		19-04-1993
-----						
WO 9628543	A	19-09-1996	DE	19532906 A		19-09-1996
			AU	702514 B		25-02-1999
			AU	5106696 A		02-10-1996
			BR	9607143 A		25-11-1997
			CA	2213723 A		19-09-1996
			CZ	9702803 A		15-04-1996
			EP	0815211 A		07-01-1998
			JP	11501517 T		09-02-1999
			NO	974260 A		14-11-1997
			PL	322271 A		19-01-1998
-----						

EPO FORM P459

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

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